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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,187	07/30/2003	Jurgen Engel	103832-477-NP	9817

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GOODWIN PROCTER LLP
599 Lexington Avenue
New York, NY 10022

EXAMINER	
DELACROIX MUIRHEI, CYBILLE	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/632,187	ENGEL ET AL.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *5-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/28/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Claims 1-12 are presented for prosecution on the merits.

Information Disclosure Statement(s)

Applicant's Information Disclosure Statement received Nov. 28, 2003 has been considered. Please refer to Applicant's copy of the 1449 submitted herewith.

Claim Objection(s)

1. Claims 5-11 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim (1) cannot depend from another multiple dependent claim and (2) should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, claims 5-11 have not been further treated on the merits.

2. Claims 1-4, 12 are objected to because of the following informalities: in claim 1, line 1, after "using", the "of" should be cancelled. Then, at line 1, the "and" between "Formula I" and "Formula II" should be cancelled and replaced with –or--. Additionally, in claim 1, at line 11, the left "(" should be cancelled and "C_3 to CO" should read -- C_3 to C_7--. Please see claim 2. Finally, in claim 1, page 11, lines 4-5, the phrase "and pharmaceutically acceptable salts and prodrugs thereof" should be deleted and inserted at line 2, after "groups."

In claim 2, line 1, the "of" after "using" should be cancelled. In claim 3, line 1, the "of" after "using" should be cancelled. In claim 4, line 1, the "of" after "using" should be cancelled. In claim 12, line 2, the "and" before "II" should be cancelled and replaced with –or--, and after "II", the phrase –as claimed in claim 1—should be inserted. Appropriate correction is required.

Claim Rejection(s)—35 USC 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-4 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-4 and 12, the limitation "approved anti-tumor medicament" renders the claims vague and indefinite. The specification does not clearly set forth explicitly and with reasonable clarity the definition of this limitation. Instead, the description at page 4, lines 11-16, "anti-tumor substances may be alkylating agents, anti-metabolites, plant alkaloids" etc. appears to be merely exemplary and does not describe what would be excluded by the limitation. Therefore, the metes and bounds of the patent protection desired are unclear, and one of ordinary skill in the art would not be reasonably apprised of the scope of the claimed method.

Claim Rejection(s)—35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. Claims 1-4, 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Nickel et al., 6,093,704.

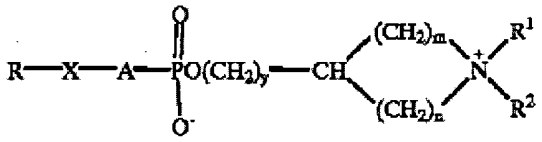
Nickel et al. disclose the invention substantially as claimed. Specifically, Nickel et al. teach anti-tumor compounds such as miltefosine or octadecyl (1,1-dimethylpiperidinio-4-yl) phosphate, wherein said compounds are used in pharmaceutical compositions or dose units (i.e. drug products) for effective treatment of cancer. Please see col. 1, lines 10-17; col. 2, lines 40-44; claims 1-2.

5. Claims 1-4, 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Nickel et al., 6,696,428.

Nickel et al. disclose the invention substantially as claimed. Specifically, Nickel et al. teach anti-tumor compounds such as miltefosine or octadecyl (1,1-dimethylpiperidinio-4-yl) phosphate, wherein said compounds are used in pharmaceutical compositions or dose units (i.e. drug products) for effective treatment of cancer. Please see col. 1, lines 13-15; col. 2, lines 40-44; claims 1-2.

6. Claims 1, 3, 4, 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Nössner et al., 6,172,050.

Nössner et al. disclose alkylphosphocholine compounds and their use in pharmaceutical compositions for treating tumors. The compounds are represented by the following General Formula (I):

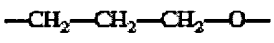


(I)

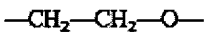
in which

R is a linear or branched alkyl radical having 10 to 24 carbon atoms, which can also contain one to three double or triple bonds, R^1 and R^2 independently of one another are hydrogen or in each case a linear, branched or cyclic saturated or unsaturated alkyl radical having 1 to 6 carbon atoms, which can also contain a Cl, OH or NH_2 group, it also being possible for two of these radicals to be bonded together to form a ring,

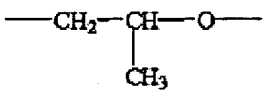
A is a single bond or one of the groups of the formulae



(II),

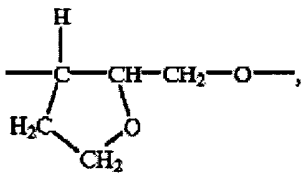


(III),



(V),

(VI)



the groups (II) to (VI) being orientated in such a way that the oxygen atom is bonded to the phosphorus atom of compound (I), X is an oxygen or sulphur atom or NH when A is a single bond, or an oxygen or sulphur atom when A is one of the groups (II) to (VI),

y is equal to 0 or a natural number between 1 and 3, and

m and n independently of one another are 0 or natural numbers, with the proviso that m+n=2 to 8.

Specific compounds which anticipate Applicant's claims are found in the Examples as well as claims 5, 6. Nössner et al. disclose that these compounds have better anti-tumor activity than the open-chain derivatives. Please see col. 1-2; col. 2, lines 55-57; Examples 5, 18-21.

Claim Rejection(s)—35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-2, 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Engel et al., 5,942,639 in view of Nickel et al., 6,093,704, supra.

Engel et al. disclose a process for making alkylphosphocholines, which are known to be used for treating tumors. Specific compounds disclosed in Example 2, cols. 6-7 are encompassed by Applicant's claims. Please also see col. 1, lines 10-15.

Engel et al. do not specifically disclose the use of these compounds in pharmaceutical compositions or drug products; however, the Examiner refers to Nickel et al., which disclose anti-tumor compounds such as miltefosine or octadecyl (1,1-dimethylpiperidinio-4-yl) phosphate, wherein said compounds are used in pharmaceutical compositions or dose units (i.e. drug products) for effective treatment of cancer. Please see col. 1, lines 10-17; col. 2, lines 40-44; claims 1-2.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the alkylphosphocholines disclosed by Engel et al. into pharmaceutical compositions/drug products containing pharmaceutically acceptable excipients because one of ordinary skill in the art would reasonably expect the resulting compositions to be useful therapeutically for treating tumors. Moreover, formulation of therapeutically active compounds into pharmaceutical compositions/drug products is an art-recognized, result-effective variable and it would have been obvious and well within the capability of the skilled artisan to optimize in the teachings of the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1, 3, 4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,172,050. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant application and USPN '050 claim

alkylphosphocholine compounds having anti-tumor activity, wherein the compounds claimed are substantially identical to those claimed in the instant application.

The claims of USPN '050 differ from the claims of the instant application in that USPN '050 specifically claims pharmaceutical compositions (i.e. drug products) containing the alkylphosphocholine compounds. The instant application claims a method for using the alkylphosphocholine compounds for the manufacture of drug products for treating tumors.

However, the use of therapeutically active compounds for the manufacture of the claimed compositions in USPN '050 would have been obvious to one of ordinary skill in the art at the time the invention was made.

9. Claim 12 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,172,050. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428. 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are generic to all that is recited in the claims 1-7 of USPN '050. That is, the claims of USPN '050 fall entirely within the scope of the claims of the instant application. In other words, the claims of the instant

application are anticipated by claims 1-7 of USPN '050. Specifically, the claims of USPN '050 recite substantially identical alkylphosphocholine compounds as those claimed in the instant application, wherein the claims recite specific compounds resulting in species of compounds, which are embraced by the claims of the instant application.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Schumacher et al., 5,219,866.

Claims 1-4, 12 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Cybille Delacroix-Muirheid** whose telephone number is **571-272-0572**. The examiner can normally be reached on Mon-Thurs. from 8:30 to 6:00 as well as every other Friday from 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Christopher Low**, can be reached on **571-272-0951**. The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CDM
Oct. 29, 2004

Cybille Delacroix-Muirheid
Patent Examiner Group 1600